INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB2005/002607

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K16/12 A61K39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, Sequence Search, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2004/094474 A (NEUTEC PHARMA PLC; BURNIE, JAMES, PETER; MATTHEWS, RUTH, CHRISTINE) 4 November 2004 (2004-11-04) see especially SEQ ID NO:s 27 and 32; the whole document	12-17
X	WO 01/27279 A (CAMBRIDGE ANTIBODY TECHNOLOGY; EDWARDS, BRYAN, MICHAEL; MAIN, SARAH, H) 19 April 2001 (2001-04-19) see especially SEQ ID NO: 62 the whole document	12-17
X	WO 01/44300 A (CAMBRIDGE ANTIBODY TECHNOLOGY LIMITED; WEBSTER, CARL; OSBOURN, JANE; W) 21 June 2001 (2001-06-21) see especially SEQ ID NO: 76; the whole document	12-17

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 August 2005	20/09/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Giebeler, K

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB2005/002607

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/96599 A (PHILOGEN S.R.L; CASTELLANI, PATRIZIA; ZARDI, LUCIANO; ZIJLSTRA, ANDRIE) 20 December 2001 (2001-12-20) see especially SEQ ID NO:4; the whole document	12-17
X	WO 03/048321 A (ALEXION PHARMACEUTICALS, INC; ROTHER, RUSSELL; WU, DAYANG) 12 June 2003 (2003-06-12) see espcially SEQ ID NO: 106; the whole document	12-17
A	WO 03/052416 A (NEUTEC PHARMA PLC; BURNIE, JAMES, PETER; MATTHEWS, RUTH, CHRISTINE; RI) 26 June 2003 (2003-06-26) cited in the application the whole document	1-32
A	WO 02/062379 A (THE PROVOST, FELLOWS AND SCHOLARS OF THE COLLEGE OF THE HOLY AND UNIDI) 15 August 2002 (2002-08-15) cited in the application the whole document	1-32
A	WINZER KLAUS ET AL: "Differential regulation of two thiolase genes from Clostridium acetobutylicum DSM 792" JOURNAL OF MOLECULAR MICROBIOLOGY AND BIOTECHNOLOGY, vol. 2, no. 4, October 2000 (2000-10), pages 531-541, XP009053009 ISSN: 1464-1801 the whole document	1-32
A	SLIWKOWSKI M X ET AL: "INCORPORATION AND DISTRIBUTION OF SELENIUM INTO THIOLASE FROM CLOSTRIDIUM-KLUYVERI" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 260, no. 5, 1985, pages 3140-3144, XP002342751 ISSN: 0021-9258 the whole document	1-32

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2005/002607

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   - [X] a sequence listing
   - [ ] table(s) related to the sequence listing

   b. format of material

   - [X] in written format
   - [X] in computer readable form

   c. time of filing/furnishing

   - [X] contained in the international application as filed
   - [X] filed together with the international application in computer readable form
   - [ ] furnished subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2005/002607

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 29-32 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 29-32 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: -

Present claims 1,2,10,11,18-20, and 28-32 relate to the use of a compound defined by reference to a desirable characteristic or property, namely to an inhibitor of acetyl-CoA acetyltransferase.
The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to those inhibitors of acetyl-CoA acetyltransferase which are antibodies or antigen binding fragments thereof.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB2005/002607

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 2004094474	A	04-11-2004	WO	2004094474 A1	04-11-2004
WO 0127279	A	19-04-2001	AU	7676300 A	23-04-2001
			WO	0127279 A1	19-04-2001
WO 0144300	A	21-06-2001	AU	770115 B2	12-02-2004
			AU	1713901 A	25-06-2001
			CA	2393292 A1	21-06-2001
			EP	1242458 A2	25-09-2002
			WO	0144300 A2	21-06-2001
			JP	2003516745 T	20-05-2003
WO 0196599	A	20-12-2001	AU	8182401 A	24-12-2001
			WO	0196599 A2	20-12-2001
WO 03048321	A	12-06-2003	AU	2002359568 A1	17-06-2003
			CA	2468744 A1	12-06-2003
			EP	1461428 A2	29-09-2004
			JP	2005511706 T	28-04-2005
			WO	03048321 A2	12-06-2003
			US	2003219861 A1	27-11-2003
			US	2004038308 A1	26-02-2004
WO 03052416	A	26-06-2003	AT	288502 T	15-02-2005
			AU	2002352394 A1	30-06-2003
			CA	2471570 A1	26-06-2003
			DE	60202877 D1	10-03-2005
			EP	1415002 A2	06-05-2004
			ES	2236605 T3	16-07-2005
			WO	03052416 A2	26-06-2003
WO 02062379	A	15-08-2002	EP	1358331 A2	05-11-2003
			WO	02062379 A2	15-08-2002
			IE	20020097 A1	28-05-2003
			US	2003054009 A1	20-03-2003

PATENT COOPERATION TREATY

- 4 JUL 2006

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WAMP101123-WO	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/GB2005/002607	International filing date *(day/month/year)* 01.07.2005	Priority date *(day/month/year)* 02.07.2004
International Patent Classification (IPC) or national classification and IPC INV. C07K16/12		
Applicant NEUTEC PHARMA PLC et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 2 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☒ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.04.2006	28.06.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer van Heusden, M Telephone No. +49 89 2399-8145

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2005/002607

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-33	as originally filed

Sequence listings part of the description, Pages

1-14	as originally filed

Claims, Numbers

1-8, 15-22, 30-32	as originally filed
9-14, 23-29	received on 12.04.2006 with letter of 11.04.2006

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. II Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
   - ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
   - ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

   see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2005/002607

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1,2,10,11,18-20,28-32

because:

☒ the said international application, or the said claims Nos. 29-32 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*.

☒ no international search report has been established for the said claims Nos. 1,2,10,11,18-20,28-32

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-32
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-11, 18-32
	No:	Claims	12-17
Industrial applicability (IA)	Yes:	Claims	1-28
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ on paper

   ☒ in electronic form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in electronic form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

Re Item II:

The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of said earlier application. This report has nevertheless been established on the assumption that the relevant date is the claimed priority date.

Re Item III:

1. The present report is only formulated with respect to those parts of the claims for which an international search report has been established, i.e. parts relating to those inhibitors of acetyl-CoA acetyltransferase which are antibodies or antigen binding fragments thereof.

2. Claims 29-32 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. In this respect the following should be noted:
For the assessment of these claims on the question whether they are industrially applicable, no unified criteria exist in PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V:

1. Novelty:

The subject matter of claims 1-32 complies with Articles 33(2) PCT.

2. Inventive step:

The subject-matter of claims 12-17 relates to specific antibodies, which antibodies apparently are reactive with *Clostridium* and *Enterococcus* acetyl-CoA acetyltransferase. It is noted that said claims are product claims which do not refer to any therapeutic application. The closest prior art to assess the inventiveness of said claims is any of documents D8 (Winzer) and D9 (Sliwkowski), disclosing the acetyl-CoA acetyltransferase of *Clostridium.* Once an enzyme is known, no inventive skill is needed to provide antibodies against said enzyme. Therefore the subject matter of claims 12-17 is not considered inventive. It seems that the inventive concept of the present application is the surprising fact that antibodies against acetyl-CoA acetyltransferase (not a surface antigen) can be used for the treatment of *Clostridium* and *Enterococcus* infection. Therefore inventive step is recognized for therapeutic applications of said antibodies, as defined in claims 1-11 and 18-32.

9. The use according to claim 3, said antibody or antigen binding fragment thereof having the sequence of SEQ ID NO: 41.

10. The use according to any of the preceding claims, the medicament additionally comprising at least one of the group of antibiotics consisting: gentamicin, vancomycin and metronidazole.

11. A combined preparation for the treatment of infection by *Clostridium difficile*, comprising:

(i) an inhibitor of acetyl-CoA acetyltransferase; and

(ii) at least one of the group of antibiotics consisting: gentamicin, vancomycin and metronidazole.

12. Isolated and/or purified antibody or antigen binding fragment thereof comprising at least one of the group consisting of:

(i) VH chain complementarity determining regions (CDRs) 1-3 having the sequences of SEQ ID NOs: 2-4 respectively; and

(ii) VL chain complementarity determining regions (CDR) 3 having the sequence of SEQ. ID NO: 19.

13. Isolated and/or purified antibody or antigen binding fragment thereof according to claim 12, said VH chain having the sequence of SEQ ID NO: 1.

14. Isolated and/or purified antibody or antigen binding fragment thereof according to either of claims 12 or 13, said VL chain having the sequence of SEQ ID NO: 16.

23. The use according to either of claims 21 or 22, said antibody or antigen binding fragment thereof having VH chain complementarity determining regions (CDRs) 1-3 having the sequences of SEQ ID NOs: 2-4 respectively.

24. The use according to claim 23, said antibody or antigen binding fragment thereof VH chain having the sequence of SEQ ID NO: 1.

25. The use according to any of claims 21-24, said antibody or antigen binding fragment thereof having VL chain complementarity determining regions (CDR) 3 having the sequence of SEQ. ID NO: 19.

26. The use according to claim 25, said antibody or antigen binding fragment thereof VL chain having the sequence of SEQ ID NO: 16.

27. The use according to claim 21, said antibody or antigen binding fragment thereof having the sequence of SEQ ID NO: 41.

28. A combined preparation for the treatment of infection by *Enterococcus faecium* or *Enterococcus faecalis*, comprising:

(i) an inhibitor of acetyl-CoA acetyltransferase; and

(ii) vancomycin.

29. A method of treatment of infection by *Clostridium difficile*, comprising administering a therapeutically effective quantity of an inhibitor of acetyl-CoA acetyltransferase to a patient in need of same.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/GB2005/002607	International filing date *(day/month/year)* 01.07.2005
Priority date *(day/month/year)* 02.07.2004	
International Patent Classification (IPC) or both national classification and IPC C07K16/12, A61K39/395	
Applicant NEUTEC PHARMA PLC	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Giebeler, K

Telephone No. +49 89 2399-8546

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1,2,10,11,18-32

because:

☒ the said international application, or the said claims Nos. 29-32 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☒ the claims, or said claims Nos. 18-28 (all partially) are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 1,2,10,11,18-20,28-32 (all partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-11,13-32
	No:	Claims	12
Inventive step (IS)	Yes:	Claims	1-11,18-32
	No:	Claims	13-17
Industrial applicability (IA)	Yes:	Claims	1-28
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III.

1. The present opinion is only formulated with respect to those parts of the claims for which an international search report has been established, i.e. parts relating to those inhibitors of acetyl-CoA acetyltransferase which are antibodies or antigen binding fragments thereof.

2. As concerns claim 18-28, 31 and 32 when referring to Enterococcus faecalis, the application does not demonstrate that treatment of infection is actually possible using antibody inhibitors of acetyl-CoA acetyltransferase. Therefore, said part of the claims lack support (Article 6 PCT) and sufficiency of disclosure (Article 5 PCT) to such an extend that no meaningful opinion can be formed.

3. Claims 29-32 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. In this respect the following should be noted:

   For the assessment of these claims on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

   Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

4. Reference is made to the following documents:
   D2: WO 01/27279 A, 19 April 2001
   D3: WO 01/44300 A, 21 June 2001
   D4: WO 01/96599 A, 20 December 2001

D5: WO 03/048321 A, 12 June 2003

5. CLAIM INTERPRETATION

Claim 18 relates to the use of an inhibitor of acetyl-CoA acetyltransferase and vancomycin in the manufacture of a medicament, and does not state that **a combination** of the two compounds is actually used. Therefore, the claim could be interpreted to cover the use of vancomycin alone, which would clearly not be novel. Since it is however apparent from the description that the applicant intends to claim the combination of the two compounds, the claim has been interpreted as relating to this combination. The present opinion is based on this interpretation.

6. NOVELTY

Antibodies comprising VL chain CDRs having the sequences of SEQ ID Nos: 17 and 18 are well-known from the prior art, see for instance the documents D2 to D5. Therefore, **claim 12** lacks novelty over each of these documents.

7. INVENTIVE STEP

7.1. The application demonstrates that the antibody H1L1, which binds to Clostridium difficile acetyl-CoA acetyltransferase, inhibits growth of C. difficile and Enterococcus faecium, whereby synergy with vancomycin and gentamycin is observed (see Tables 2 and 3). Based on these results, an inventive step can be acknowledged for claims 1-11 and 18-32.

7.2. No inventive step can be acknowledged for claims 13-17 relating to certain antibodies or antigen binding fragments thereof, since these antibodies represent merely a selection out of the numerous possibilities from which a person skilled in the art would choose when faced with the problem of providing antibodies against C. difficile acetyl-CoA acetyltransferase. It has not been credibly demonstrated that all antibodies or antigen binding fragments thereof covered by the claims show surprising, advantageous properties.